

### **REMARKS**

Claims 5, 6 and 8-15 are pending in the current application. Claim 7 has been canceled without prejudice and without acquiescence. Claim 5 has been amended to further define a cell as a cardiac cell. Claim 8 has been amended to correct dependency and to recite “cardiac cell” and Claim 9 has been amended to correct claim informalities. Support for these amendments can be found in the claims as originally filed and throughout the specification as a whole, particularly at paragraphs [0011] and [0023]. Applicants assert that no new matter has been added.

Issues outstanding in the pending application are as follows:

- Claim 9 is objected to because it contains informalities.
- Claim 15 is objected to under 37 CFR § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.
- Claims 5-15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Drewett *et al.* (Journal of Biological Chemistry. 2001. Vol.276; No.36: 33444-33451) in view of Narula *et al.* (PNAS. July 1999. Col.96:8144-8149).

#### **I. Informalities**

A. Claim 9 is objected to because of the following informalities: The Examiner does not believe that the phrase, “is further defined as” adequately captures the intended meaning of the applicant, and suggests, “further comprises” or “is further comprised of.” Applicants have amended claim 9 to comply with the Examiner’s suggestion.

B. Claim 15 is objected to under 37 CFR § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicants respectfully traverse.

As stated on page 4 of the pending Office Action, the Examiner fails to see how redefining “cardiac disease” to mean “cardiac failure” further limits the claimed method, that

at best it would be a change in scope of the intended use. However, Applicants' assert that cardiac disease and cardiac failure have two distinct meanings and that cardiac failure is one of several possible cardiac diseases. Both terms are clearly defined in the Applicants specification at paragraphs [0034] and [0035]. Paragraph [0035] defines cardiac disease as a medical condition related to the cardiovascular or circulatory system, and lists several contemplated cardiac or cardiovascular diseases, one of which is heart (or cardiac) failure. Therefore, Applicants assert that cardiac failure in claim 15 properly further limits cardiac disease of claim 1.

In light of the above argument, Applicants respectfully request that the objection be withdrawn.

## **II. 35 U.S.C. § 103(a)**

Claims 5-15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Drewett *et al.* (Journal of Biological Chemistry. 2001. Vol.276; No. 36: 33444-33451) in view of Narula *et al.* (PNAS. July 1999. Col. 96: 8144-8149). Applicants respectfully traverse.

The Examiner has asserted that one of ordinary skill in the art would have been motivated to combine Drewett *et al.* and Narula *et al.* because both references indicate a link between apoptosis and disease states. Narula *et al.* indicate the relationship between apoptosis and heart failure, while Drewett *et al.* describe the relationship between SRF cleavage and apoptosis (page 7 of the pending Office Action). However, to establish *prima facie* obviousness the Examiner must identify and explain the reasons why one of ordinary skill in the art would have derived the claimed subject matter and why one of ordinary skill in the art would have a reasonable expectation of success, which the Examiner has failed to do. *KSR International Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 1741, 167 L. Ed. 2d 705, 722 (U.S. 2007) ("[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness," quoting *In re Kahn*, 441 F. 3d 977, 988 (Fed. Cir. 2006)); *Dystar Textilfarben GmbH v. C.H. Patrick Co.*, 464 F.3d 1356, 1360-61 (Fed. Cir. 2006); *In re Lee*, 277 F.3d 1338, 1341, 1344-45 (Fed. Cir. 2002); *See also* Memorandum from Margaret A. Focarino et al. to Technology Center Directors re Supreme Court Decision on *KSR Int'l Co. v. Teleflex, Inc.* (USPTO May 3, 2007). Drewett *et al.*

discloses cleavage of SRF and apoptosis in human BJAB cells (Drewett *et al.*, abstract) and one of ordinary skill in the art would have no expectation that these results would be similar in any cell other than BJAB cells. However, in order to advance prosecution, claim 1 has been amended to specifically recite cardiac cells. The Examiner has not indicated why a person of ordinary skill in the art would have any reasonable expectation that the cleavage and apoptosis in BJAB cells would occur in any other cell type, particularly the cardiomyocytes of Narula or cardiac cells of the presently amended claims.

In addition, at the time of filing, the state of the art was such that it was believed that the fragments of SRF associated with cardiac disease were alternatively spliced and not cleaved. This is evidenced by the IDS-submitted publication by Davis *et al.* which describes an SRF isoform encoded by an alternatively spliced form of SRF lacking exons 4 and 5 of the SRF primary RNA transcript (SRF- $\Delta$ 4,5), and states, “these results suggest that expression of SRF- $\Delta$ 4,5 in failing hearts may in part contribute to impaired cardiac gene expression and consequently to the pathogenesis of heart failure.” (Davis *et al.*, abstract). As evidence of the state of the art at the time of filing, Applicants note that Applicants’ publication (Chang *et al.*, 2003; submitted in an IDS filed July 17, 2007) describing the invention. Chang *et al.* was published after the filing date but describes the state of the art at the time of filing, particularly that Davis *et al.* described SRF fragments in the failing heart and ascribed these fragments as alternatively spliced SRF transcripts, as described above (Chang *et al.*, page 412, column 2). Both Davis *et al.* and Chang *et al.* provide evidence that one of skill in the art, armed with the knowledge available in the art at the time of filing, would have believed that alternatively spliced SRF fragments were associated with cardiac disease and would not have expected the cleavage of SRF and apoptosis in BJAB cells as taught in Drewett *et al.* to be applicable to cardiac cells. Therefore, the skilled artisan would not have found it obvious that cleavage of SRF would be associated with heart disease. This is especially true in light of the publication dates of both Drewett *et al.* (September 2001) and Davis *et al.* (December 2001). Because Davis *et al.* was published several months after Drewett *et al.*, it would have been the most up-to-date reference prior to filing of the present application and would have been seen as describing the most current knowledge at the time of filing (*i.e.* that alternatively spliced, not cleaved, SRF fragments were associated with heart disease).

Therefore, Applicants assert that the claimed invention is not obvious in light of the proposed combination of Drewett *et al.* and Narula *et al.*. Applicants further assert that the Examiner has not made a *prima facie* case of obviousness by failing to provide articulated reasoning why one of skill in the art would have had reasonable expectation that the proposed combination would have been successful in light of the knowledge of one of skill in the art at the time of filing. In light of the above arguments, Applicants respectfully request that the rejection be withdrawn.

### **CONCLUSION**

In view of the above, Applicant believes the pending application is in condition for allowance.

Applicant believes no fee is due with this response other than the fee for the Supplemental Information Disclosure Statement. However, if a fee is due, please charge Deposit Account No. 06-2375, under Order No. HO-P02659US1 from which the undersigned is authorized to draw.

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Respectfully submitted,

By /Melissa L. Sistrunk/  
Melissa L. Sistrunk  
Registration No.: 45,579  
FULBRIGHT & JAWORSKI L.L.P.  
Fulbright Tower  
1301 McKinney, Suite 5100  
Houston, Texas 77010-3095  
(713) 651-5151  
(713) 651-5246 (Fax)  
Attorney for Applicant